Reactive Oxygen Species Production by Differentiated Monocytes (THP-1) : Efficiency and Evaluation of Antioxidant Profile of some Anti-inflammatory Drugs.

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Atherosclerosis, one of the most disabling disease in the western countries, is responsible for half of adult deaths in the United States (1). Human monocytes and the infectious agent, *Chlamydia pneumoniae,* were demonstrated to play a role in this disease by the way of low density lipoprotein (LDL) oxidation (2). It was also demonstrated that cyclooxygenase-2 (COX-2) is widely expressed in atheroslerotic lesions (3). We recently demonstrated that differentiated human monocytes (THP-1 cell line), after incubation with *Chlamydia pneumoniae*, were able to induce oxidative processes via the NADPH oxidase pathway (4). Consequently, modulation of inflammatory and oxidative processes by pharmacological tools constitute the exciting challenge.

Herein, we reported the effects of a series of COX-2 inhibitors on the oxidative process of THP-1 cells differentiated by incubation with *C. pneumoniae*. Cox-2 inhibitors were compared to classical anti-inflammatory drugs. Complementary biochemical analyses were performed by in vitro system. Four techniques were used : i) free radical production was monitored by electron spin resonance (ESR) spin trapping ; ii) activated species were evidenced by luminol or lucigenin-enhanced chemiluminescence (CL), iii) the respiratory function (oxygen consumption) was assessed by oxymetry and iv) the role of H_2O_2 in the last step of oxidative processes was evidenced by measuring ethylene (oxidation of γ-keto-methyl butyric acid; KMB) escape using gas chromatography.

By ESR spin trapping technique, we demonstrated that the production of superoxide radicals by PMA-activated macrophages (6.10^6 cells/ml) was inhibited by 10 µM NS-398, celebrex and 4'HO-nimesulide while indomethacin, aceclofenac and diclofenac were without effects. Similarly, at the concentrations of 10 µM and 100 µM, a decrease of CL was observed (10, 28, 74% of decrease, respectively). Ibuprofen (10 and 100 µM) did not affect CL while the ESR spectrum intensity was dose-dependently decreased. A correlation was found between reactive oxygen species production, oxygen consumption and ethylene escape and the effect of studied molecules will be discussed in term of structure-activity relationships.

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